GUINEA PIG ILEUM

Prostaglandins:

prostaglandins, type E: | (1) synthesized and released from ileum
prostacyclin : | (2) contract longitudinal smooth muscle
| (3) increase ACh output from nerve endings
max. contraction with ACh: 0.4 umol/l

Atropine:

specific antagonist of muscarinic receptors, 1 to 30 nmol/l

Physostigmine:

prevent hydrolysis of ACh by inhibition of ChE, 50 nmol/l

Hemicholinium-3:

competitive inhibition of choline uptake into nerve endings

Tetradoxin:

blocking of sodium channels in nerve cells but not in smooth muscle cells

Beta-bungarotoxin:

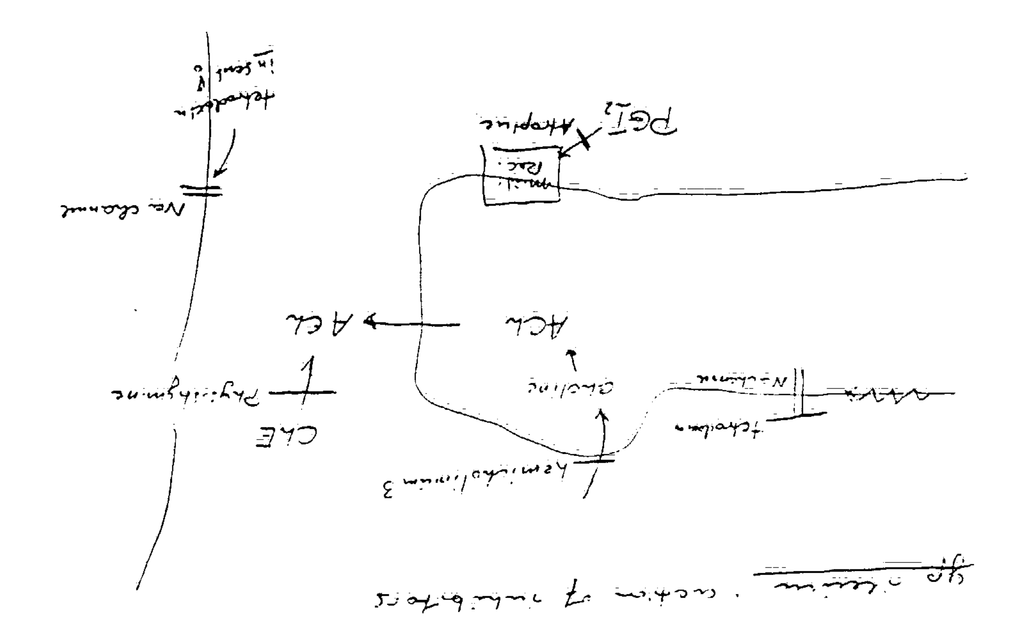
abolishes ACh release in somatic motor nerves and parasympathetic fibres
guinea pig ileum: only partially sensitive to parasympathetic blocking action

Hexamethonium:

ganglionic blocker, competitive antagonist on nicotinic receptor without affecting transmitter release

(Gaion, R.M, and Tranto, M., The role of prostacyclin in modulating cholinergic neurotransmission in guinea pig ileum, Br. J. Pharmac. 80: 279-286 (1983))

2028916538



action of inhibitors
hemicholinium 3
choline
ACh
ACh
ChE
Na channel
Rec.
PGI$_2$
Atropine

H

2028916539

HALOTHANE
=========

Side Effects:

severe attacks provoked in malignant hyperthermia patients.
(Berg, K. (ed.): Genetic damage in man caused by environmental agents, New York: Academic Press, 1979, BC 71)

Mucociliary Transport:

decreased rate
(Forbes et al., Anesthesiology 46 : 319 (1977))

8.Aug.83 GD14 (LIT) B15

HASHISH (CANNABIS)
==================

Hallucinogen:

delta 9-tetrahydrocannabinol

Effects:

psychical

HEINZ BODIES

Morphology:

dark-staining granules found in erythrocytes near interior surface of membrane. Consist of denatured hemoglobin, possibly sulfhemoglobin

Attachment to membrane SH groups results in impairment of membrane function (hyperpermeability, hemolysis).
(Smith, R.P., Toxic responses of the blood in Casaret and Doull (eds.): Toxicology, the basic science of poisons, 2nd edition, New York: Macmillan Publishing Co., Inc., 1975, pp 311-331 (page 326))

Toxicological Relevance:

indication for oxidative stress
(Smith, R.P., Toxic responses of the blood in Casaret and Doull (eds.): Toxicology, the basic science of poisons, 2nd edition, New York: Macmillan Publishing Co., Inc., 1975, pp 311-331 (page 326))

Agents Producing HB:

phenols (keyword),
aniline,
nitrobenzene,
ascorbic acid
(Smith, R.P., Toxic responses of the blood in Casaret and Doull (eds.): Toxicology, the basic science of poisons, 2nd edition, New York: Macmillan Publishing Co., Inc., 1975, pp 311-331 (page 326))

Species Differences:

highly responsive: cat
mouse
dog
human
less responsive : guinea pig,
rabbit,
monkey
(Smith, R.P., Toxic responses of the blood in Casaret and Doull (eds.): Toxicology, the basic science of poisons, 2nd edition, New York: Macmillan Publishing Co., Inc., 1975, pp 311-331 (page 326))

GD59 (S) A3

HEMOLYSIS
=========

Detection Limit for Optical Inspection:

o.2 g/1
(Behrendt, H., Chemistry of erythrocytes, Thomas, Springfield 1957)

GD6o (S) A26

HEPARIN

=======

Anticoagulant Action:

(1) inhibition of thrombin formation
(2) inhibition of fibrin formation
active in vitro and in vivo (Buddecke, E.: Grundriss der Biochemie, 2nd ed., Berlin: Walter de Gruyter & Co., 1971, pp. 4o7-4o8)

Inactivation:

in vivo: heparinase or injection (i.v.) of protamine (Buddecke, E.: Grundriss der Biochemie, 2nd ed., Berlin: Walter de Gruyter & Co., 1971, pp. 4o7-4o8)

Lung Perfusion:

rat: heparin in perfusate activates pulmonary lipoprotein lipase (Tierney, D.F. et al., Fed. Proc. 36 : 161-165, 1977)

7.Apr.83 GD97 (S) A29

HEPATITIS B VIRUS

Occurence:

tropical and subtropical areas of Africa, South East Asia and South America
(De The, G., Viruses and human cancers - is prevention foreseeable?, ECP 1st Meeting of the Scientific Advisory Committee: 7-1o (1981))

Oncogenic Sequence:

(1) early infection (possibly transplacentally) leading to chronic carrier state
(2) cirrhosis
(3) primary liver carcinoma
(De The, G., Viruses and human cancers - is prevention foreseeable?, ECP 1st Meeting of the Scientific Advisory Committee: 7-1o (1981))

GD55 (S) B1

HEPATOCYTES

Preparation:

perfusion of liver with collagenase

Viability:

.GT.24o min

Induction of Drug Metabolism:

	PB:	3-MC:
NADPH-Cyt.c.Red.	+	o
P-45o	+	+
EH	+	?
Glucuronosyl tr.	+	+
GSH-tr.	+	?
Gamma-Glu-tr.	+	o
diaphorase	o	+

((Orrenius, S., Naunyn-Schmiedeberg's Arch. Pharmacol. 313 S: R4/16, 198o)

2028916546

22.Mar.83 (WS) GD55 (S) B28

HIND LIMB
=========

Glucose Uptake:

dependent upon blood flow, esp. important in stimulated muscle, when uptake is increased at constant glucose and insulin concentration. Linear dose response in the range of 5 to 8o micromol glucose delivery/(min x 1o g WW) (Schultz, Th.A. et al., Life Sciences 2o: 733-736, 1977)

investigation of dose response dependent upon glucose (5 to 6o mmol/l) and insulin (o to 1oooo microunits/ml) concentration in 1 pass perfusion, 3o min, unstimulated

Glucose uptake correlated with insulin concentration.

(Lewis, S.B., Schultz, T.A., Westbie, D.K., Gerich, J.E. and Wallin, J.D., Insulin-glucose dynamics during flow-through perfusion of the isolated rat hindlimb, Horm. Metab. Res. 9: 19o-195, 1977+)

Insulin:

threshold effect: 5o ul/ml must be exceeded to stimulate glucose uptake.

In presence and absence of insulin, glucose uptake was positively correlated with glucose concentration up to 3o to 45 mmol/l.

Insulin (at least immunoreactive insulin) is reduced in the perfusate during perfusion: 16 o/o reduction over the range of 5o to 1oooo uU/ml).

Effect not due to insulinase.

(Lewis, S.B., Schultz, T.A., Westbie, D.K., Gerich, J.E. and Wallin, J.D., Insulin-glucose dynamics during flow-through perfusion of the isolated rat hindlimb, Horm. Metab. Res. 9: 19o-195, 1977+)

GD27 (S) A19 (PW)

HISTOLOGY

Definitions:

metaplasia :	Gewebsumwandlung
hyperplasia:	Vergrösserung eines Organs, Zunahme der Zellzahl
neoplasia :	(bösartige) Geschwulst
paraplasia :	Zwischenzellmasse
dysplasia :	morphol. Zellumwandlung

2028916548

GD57 (S) A7

HISTONES
========

most lysyl residue amino groups are acetylated (Jackowski, G., Liew, C.C., Analyt. Biochem. 1o2: 321-325, 198o)+

HYDRACINE
=========

Carcinogenicity:

Hydracine and most of its derivatives should be regarded as carcinogenic
(Toth, B., Cancer Res. 35: 3693 (1975))

carcinogenicity posibly related to methylation of DNA (7-methylguanine, O6MG). Methyl moiety originates from SAM (SAM can methylate DNA non-enzymatically)
(Barrows, L.R., Shank, R.C. and Magee, P.N., S-Adenosylmethionine metabolism and DNA methylation in hydrazine-treated rats, Carcinogenesis 8: 953-957 (1983))+

pulmonary tumors (mu)
liver tumore (low incidence) (rt)
(CaD, p. 102)

Mutagenicity:

Positive in Ames test
(Cancer Letters, 12: 279-285 (1981))

GD55 (S) A13

HYDROGEN PEROXIDE
=================

Determination:

assay with glucose oxidase and dyes: sensitivity 2 to 2o micro-moles/l (Ngo, T.T., Lenhoff, H.M., Anal. Biochem. 1o5: 389-397, 198o) +

26.Nov.82 GD97 (S) B1o WS

HYPERPLOIDIE
============

Definition:

genet Bez. für Zellen oder Individuen mit einem um ein oder mehrere Chromosomen oder Chromosomensegmente vermehrten Chromosomensatz, z. B. hyperhaploid, -diploid (Reallexikon der Medizin).

18.May 83 GD1o3 (S) A3 WS

HYPOTHERMIC EFFECT
=================

Smoking:

1 degree of reduction of body temperature reduced brain and (mu) liver protein synthesis by 8 o/o
(Sershen, H., Reith, M.E.A., Lajtha, A. and Gennaro, J., Effect of cigarette smoke on protein synthesis in brain and liver, Neuro-pharmacol. 2o: 451-456, 1981+)

GD59 (S) B2

HYPOXIA
=======

Perfused Lung:

95 o/o N_2, 5 o/o CO_2 = perfusate PO_2: 18 Torr, PCO_2 : 34 Torr. responses: formation of aendema, increase of 3H-Sorbitol space and lactate production, decrease of ATP, glycogen Phe incorporation. glucose uptake unaffected ((Watkins, C.A., Rannels, D.E., J. Appl. Physiol. Respir. Env. 47 : 325, 1979)

Lysosomes:

swelling and vacuolization

2028916555

IMMUNE COMPLEXES

Biological Activity:

simular to lymphokines, i. e. chemotactic for PMN's (s. TABLE 25, Vorlaender, K.-O. (ed.): Immunologie, Stuttgat: Georg Thieme Verlag, p. 439, 1983, LI-Code: MED 104). This may be relevant for TS effects in the lung.

Binding to Monocytes/Macrophages:

via Fc-receptors

Determination:

circulating IC: precipitation with PEG, analysis with anti-IgA, IgG, C3 (double diffusion)
(Gulati et al., Angiology 35 : 276-281 (1984))

Smoking:

higher protein concentration in PEG precipitates of smokers as (hu) compared to nonsmokers, no difference in constituants
(Gulati et al., Angiology 35 : 276-281 (1984))

GD6 (LIT) B28

IMMUNOELECTROPHORESIS
====================

increasing the sensitivity of the technique by the use of fluorography of specially prepared agarose gels (Noren, O., Sjöström, H., Biochem. Biophys. Methods 1: 59-64, 1979)

GD14 (LIT) B2

INFUSION
========

Long-term Infusion Technique

A technique is described that allows tail vein infusions in the rat up to several weeks without the risk of pressure necrosis of the tail. By the aid of a simple metallic device the catheter is protected against damage by the animal. Since this armament is well tolerated and the mobility of the rat remains unimpaired, psychic stress is minimized.

Arzneim.-Forsch./Drug Res. 27 (I), 864 (1977)

2028916558

INHIBIN
=======

Function:

gonadal water-soluble hormone, which can selectively suppress the release of FSH from pituitary gland
(de Jong, Molec. Cell Endocr. 13: 1-1o, 1979)

INITIATORS

Basic Properties:

(1) At sufficient dosages usually carcinogenic by themselves, i. e., serve as "solitary carcinogens"

(2) At lower doses that are not carcinogenic or are only weakly carcinogenic ("subthreshold" or "threshold" , "initiation", resulting in a cryptic state, manifested by fact that subsequent exposure of the initiated tissue to promoting agents leads to the occurence of benign and malignant skin tumors. At present no specific morphological or biochemical feature has been identified with the process of initiation. It probably involves somatic cell mutation, although a stable epigenetic change has not been excluded.

(3) Single exposure to the agent sufficient for initiation

(4) Initiation appears to be a rapid, irreversible process, since application of the promoting agent can be delayed for many months (up to 7o weeks, Yuspa, S.H., Hennings, H., Saffiotti, U., Cutaneous chemical carcinogenesis: past, present and future, J. Invest. Dermatol. 67: 199-2o8 (1976+) and cancers will still be induced.

(5) There does not appear to be a threshold dose below which the initiating effect is completely lost.

(6) Administration of 2 initiating agents or repetitive small doses of the same agent appears to be additive.

(7) Most initiating agents either generate or are metabolically converted to electrophilic reactants, which bind covalently to cellular DNA and other macromolecules. Their activated forms are generally mutagenic.

(Weinstein, B., Troll, W., Cancer Research 37: 3461-3463, 1977)

Skin Initiators:

(mu)

MNNG,
beta-propionolactone,
DMBA, DBA,
MC,
4-nitroquinoline-1-oxide,
B(a)P
Yuspa, S.H., Hennings, H., Saffiotti, U., Cutaneous chemical carcinogenesis: past, present and future, J. Invest. Dermatol. 67: 199-2o8 (1976+)

GD6 (LIT) B29

IODINATION OF PROTEINS

Relative Efficiencies of Methods of Radioiodination:

sodium iodide with chloramine-T, sodium iodide with "iodogen" and the Bolton and Hunter reagent, have been compared. The results obtained for the labelling of human spleen ferritin indicate that the techniques involving chemical oxidation (chloramine-T and "iodogen") cause sufficient structural alteration of the protein to change its behaviour; the Bolton and Hunter reagent does not. Similarly, the immunological activity of the labelled proteins varied; binding of the Bolton and Hunter conjugate was .GT.9o o/o whereas binding of the other products was only 6o to 8o o/o. These results confirm earlier reports that the Bolton and Hunter reagent is a very mild but effective method for the radioiodination of proteins.

Mechanism:

Under some conditions and for certain proteins, it is mainly the lysine residues which are labelled by Bolton and Hunter reagent. (Bolton, A.E. et al., Clin. Chem. 25: 1826-183o, 1979) (Knight, L.C., Welch, M.J., Biochim. Biophys. Acta 534: 185-195, 1978)

14.Jun.82 GD2 (LIT) A9 WS

ISCHEMIA
========

Definition:

In contrast to anoxia no perfusion of tissue. Requires extensive exogeneous temperature equilibration.

2028916563

KALLIKREIN
==========

- pancreatic protease, acting on alpha 2-globulin to release bradykinin
- kininogen to release kinins, which can transiently decrease the rate of ciliary beat in rabbit trachea (Lamblin et al., C.R. Soc. Biol. (Paris) 166: 618-621, 1972)

inhibitor of pancreatic trypsin (Buddecke, S. 424)

Occurence:

pancreas,
salv. glands,
intestinal mucosa,
tongue,
blood plasma (Buddecke, S. 347)
alveolar macrophages (Rylander, BGA,1984)

Inactive Proenzyme in Plasma:

pre-kallicrein, kallicreinogen (Buddecke, S. 347)

Function:

chemotactic for neutrophils (action inhibited by alpha-macroglobulin)

5.Jul.83 GD1o (LIT) B16 WS

KALLIKREIN
==========

- protease, acting on alpha 2-globulin to release bradykinin
- kininogen to release kinins, which can transiently decrease the rate of ciliary beat in rabbit trachea (Lamblin et al., C.R. Soc. Biol. (Paris) 166: 618-621, 1972)

Inhibitor of pancreatic trypsin (Buddecke, S. 424)

Occurence:

pancreas,
salv. glands,
intestinal mucosa,
tongue,
blood plasma (Buddecke, S. 347)

Inactive Proenzyme in Plasma:

Pre-kallicrein, kallicreinogen (Buddecke, S. 347)

L

GD13 (LIT) B28 (PW)

LACTIC ACID
===========

Accumulation:

cause of metabolic acidosis

Storage:

only as protein-free blood supernatant (danger of glucose metabolism), may be prevented by Na-fluoride (1o mg/ml).

Perchloric acid supernatant: stable for .GT. 1 week at o to 5 degrees centigrade (Sigma Technical Bulletin No. 726, 1977+)

Normal range:

o.3 to 1.3 mmol/l, fasting venous blood (increase during exercise) (Sigma Technical Bulletin No. 726, 1977+)

2028916567

GD11 (LIT) B14 WS

LARYNX HISTOLOGY
================

ventral depression:	cuboidal epithelium
middle part:	squamous ep.
part adjacent to pharynx:	ciliated ep.
(pharynx:	conified squamous ep.)

GD1o (LIT) B7

LAURELL-IMMUNOELECTROPHORESIS
============================

Artifacts:

(1) doubling of arcs:
movement of component in dimension 2 not at right angle to Ab-containing gel

(2) rounding of arcs:
incomplete electrophoresis
(Ryley, H.C., Biochim. Biophys. Acta 271: 3oo-3o9, 1972+)

LEIOMYOME
=========

Bösartige Tumore der glatten Muskulatur

benign tumors (expansive, compressed) of the smooth muscles of the uterus

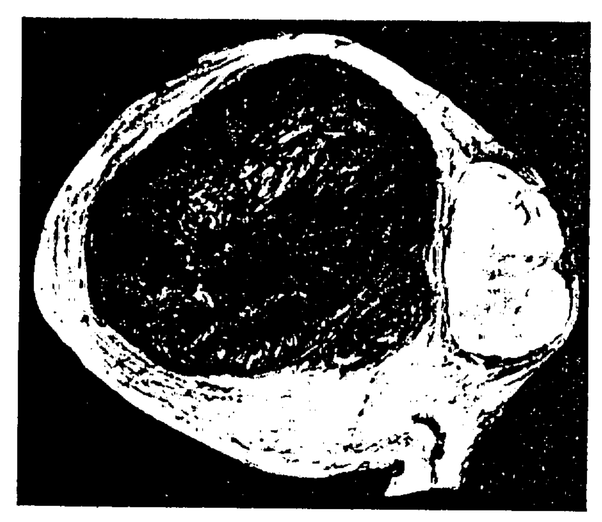


Abb. I. Uterus mit 2 Leiomyomen, Beispiel gutartigen Tumorwachstums

Grundmann, E., Das Wesen des malignen Wachstums, Klin. Wochenschr. 59: 931-941 (1981)

LEUCOCYTES (1)
==========

Pseudoeosinophils:

occurence in rabbits but not in guinea pigs (Vortrag Wissler, Biochemie Bad Nauheim, Jan.80) (rb, gp)

Invasion of Lung:

cells locate gaps between endothelial cells and move by diapedesis through them into tissues. (Athens in: Gordon, A.S. (ed.): Regul. of hematopoiesis, pp. 1143-1166 (1970))

Influence of Lung Lavage:

lavages are often followed by a massive transient increase of PMN (Cohen, A.B. (1979) L93/B12) (s. "Lavage")

Smoking:

smokers have high leukocyte counts and more neutrophiles in lavages (Helman and Rubenstein (1975) = ref. 24 in Cohen, A.B. (1979) L93/B12)

Neutrophilia (and lymphophenia) in the blood of male smokers as compared to nonsmokers, similar effect to stress-exposed humans. No studies known on nicotine, which may cause these effects (Nolle (1975) L18/B20)

Proteases:

(1) major: elastase, inhibited by alpha 2-macroglobulin (keyword), alpha-1-antitrypsin (keyword) and antileucoprotease (=)
(2) minor: collagenase, inhibited by alpha-2-macroglobulin

Chemotaxis:

important role by arachidonic acid metabolites (HETEs and HPETEs) (Capdevila, J. et al., Proc. Natl. Acad. Sci. 79 : 767-770 (1982)+)

6.Nov.84 GD13 (LIT) A4 (RZ)

LEUCOCYTES (2)
==========

Lung Air Space Content (alveolar PMN):

morphometry: 0.96E6 PMN/rabbit (rt
42 0/0 could be removed by lavage
2.5 0/0 lavaged cells = PMN (Cohen (1979) L4/D3)

Diquat:

3 days after i. p. administration transient rise in lung air space PMN (Coulombe (1984) L136/B1)

LEVANISOL
=========

Pharmacological Action:

weak immunostimulation on T-cells

LIDOCAINE
=========

Synonyms:

Lignocaine

Pharmacol. Action:

Local anaesthetic
beta-blocker

Organ Distribution:

Concentrated in the lung
(Benowith, N. et al., Clin. Pharmac. Ther. 16 : 87-98, 1974)

Detachment of Macrophages:

mouse periton. macr.: 12 mM = 3o o/o detachment, but vacuolation
(Wood, P.R. et al., J. Immun. Methods 28 : 117-124, 1979)

Determination:

TLC, analysis of fluorescence
(Seminar TLS/HPTLC, Essen, Dez.79, lecture Hetzel)

Topical Anesthetic Solution:

name: xylocaine, contains lidocaine (2 o/o) plus methyl parahydroxy-benzoate (o.1 o/o) as a preservation agent.
(Bladier, D. and Perret, G., Comparison of three methods for the determination of protein content of human broncho alveolar lavage fluids: a statistical study on 235 samples, IRCS Medical Science 1o: 1o47-1o48 (1982))

LIGANDIN
========

(Nebert et al., Proc. Natl. Acad. Sci., Vol. 76, 11: 5929-5933, 1979+)

Function:

soluble transport protein for organic anions in liver and kidney, structurally identical to GSH-S-transferase B (keyword)

Ligandin does not appear to be directly related to anion transport in the intestine. (rt)
(Manis and Apap (79), L2B13)

important for anion transport from plasma into the liver, binds also azodyl carcinogens and corticosteroids
(CaD, p. 40)

LIPIDS

Determination by TLC:

separation of serum-lipids (triglycerides, phsopholipids, cholesterol) (Kupka, J. Chromat. 146: 261, 1978)

also experiments at univ. of Bonn (Seminar TLC/HPTLC, Essen, Dez. 1979, lecture Hetzel)

Cigarette Smoking:

rat serum, 4 month exp. = increase (Mikhail, M.M. et al., Pharmazie 34: 95-96, 1979)

human, both sexes: increase (Athero-Selerosis 21: 61, 1975)

Staining:

sudan black B (o.3 o/o in 7o o/o alcohol, 5 min staining, counterstaining with o.25 o/o Safranin o for 5 to 1o s).

mitochondria react also with stain (Warr, G.A., Martin, R.R., J. of the Reticuloendothel. Society 23: 53-62, 1978)+

4.Feb.87 GD15LITB23

LIPOPOLYSACCHARIDE (LPS)
======================

Activation of Complement:

via alternative pathway

Activation of B-Lymphocytes:

- does not require T-cells
- direct binding to B-cell mitogen receptor
- high dose induces differentiation and proliferation, low dose differentiation (via LPS-Ig-receptor) only
- predominantly IgM production

(Vorlaender, K.-O. (Ed.): Immunologie, Stuttgart: Georg Thieme Verlag, 1983, p. 46, LI-Code: MED 194)

Macrophages:

LPS administration increases microbicidal activity.
Macrophages enlarge, adhere rapidly to glass, form extensive Golgi complexes, and increase number of mitochondria and lysosomes.

Sources:

E. coli
Enterobacter aglomerans (RRY)

Sensitization:

i. p. administration causes hepatotoxicity ("gal. hepatitis") and 100000 sens. to LPS

Assay:

Limulus lysate assay, detection limit: 1 pg = 30 pmol LPS

Phagocytosis:

pretreatment of mice with LPS causes 4-fold increase of phagocytosis by peritoneal macrophages

2028916577

Proc. Natl. Acad. Sci. USA
Vol. 83, pp. 5817–5821, August 1986
Biochemistry

→ LPS

Bacterial lipopolysaccharides, phorbol myristate acetate, and zymosan induce the myristoylation of specific macrophage proteins

(protein acylation/arachidonic acid metabolism/protein kinase C/signal transduction/membrane attachment)

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Contributed by Zanvil A. Cohn, April 22, 1986

ABSTRACT We demonstrate stimulus-dependent incorporation of exogenously added [^{3}H]myristic acid into specific macrophage proteins. In control unstimulated cells an 18-kDa protein is the major acylated species. In cells incubated with bacterial lipopolysaccharide (LPS), or its monoacyl glucosamine phosphate derivative, fatty acid is incorporated into proteins with molecular mass of 68 kDa and a doublet of approximately 42–45 kDa. Phorbol 12-myristate 13-acetate (PMA) or a phagocytic stimulus (zymosan) promotes the acylation of a similar array of proteins. However, PMA and zymosan also promote the myristoylation of unique proteins of [illegible] and 50 kDa. The fatty acid associated with each of the acylated proteins is myristic acid. The myristate is probably linked to the proteins through amide bonds, since it is not released by treatment with hydroxylamine. Palmitate and arachidonate are not incorporated into proteins in the same manner. Temporal analysis revealed that LPS-induced proteins are myristoylated by 30 min, while the 50-kDa protein myristoylated in response to PMA is labeled later. Most myristoylated proteins appear to be associated with the membrane fraction. Macrophages from C3H/HeJ mice, which do not respond to LPS, do not show any LPS-dependent protein acylation. Interestingly, zymosan and PMA induce the myristoylation of the 50-kDa protein in C3H/HeJ macrophages, but not the acylation of the 68-kDa and 42-kDa doublet species. We suggest that myristoylation of specific proteins is an intermediary in the capacity of LPS, PMA, and zymosan to alter macrophage functions such as arachidonic acid metabolism.

A major mechanism whereby macrophages mediate inflammation is through the secretion of arachidonic acid (20:4) metabolites (1). When murine resident peritoneal macrophages interact with zymosan particles or with phorbol 12-myristate 13-acetate (PMA) they secrete 20:4 metabolites (2, 3). We have recently shown that treatment of cells with bacterial lipopolysaccharide (LPS) increases the maximal amount of 20:4 release induced by zymosan or PMA and eliminates the lag phase of the response seen with zymosan or PMA alone (4). The active moiety of LPS, lipid A, contains a 3-OH-myristic acid moiety that has been shown to be important in LPS-induced responses (5, 6). Since acylation of select proteins has been described in several cell types (7, 8), we considered the possibility that the acylation of macrophage proteins with the 3-OH-myristic acid moiety of LPS is involved in the effect of LPS on 20:4 release by macrophages. Our first approach was to determine whether stimulation of macrophages resulted in the incorporation of exogenous [^{3}H]myristic acid into specific proteins.

Two general protein acylation reactions have been reported. The first involves the palmitoylation of proteins via ester bonds (review, ref. 9) and the other the amide linkage of myristic acid to proteins (10–14). Many of the proteins that have been shown to have the capacity to be myristoylated are important in cellular regulation, including the catalytic subunit of the cAMP-dependent protein kinase (10), calcineurin B (a component of a calmodulin-binding phosphatase) (11), the pp^{56} tyrosine kinase (12), and the pp60^{src} tyrosine kinase (13, 14). Although the function of the myristic acid moiety in these acylated proteins is unknown, it has been shown in the case of the pp60^{src} to promote the association of the tyrosine kinase with membranes and is required for its transformation properties (13, 14). → TPA

In this report we demonstrate that specific proteins are acylated with exogenous myristic acid when macrophages are stimulated with LPS, zymosan, or PMA.

MATERIALS AND METHODS

Macrophage Cultures. Primary cultures of peritoneal macrophages were established from resident cells of specific pathogen-free female ICR mice (Trudeau Institute, Saranac Lake, NY) or from C3H/HeJ mice (The Jackson Laboratory) as previously described (15). Peritoneal cells (approximately 9×10^6 per ml) in α modified minimal essential medium (α-MEM; GIBCO) containing 10% fetal calf serum were cultured in 35-mm-diameter plastic culture dishes (1 ml per dish). After 2 hr at 37°C in 95% air/5% CO_2, cultures were washed three times in calcium- and magnesium-free phosphate-buffered saline (PD) to remove nonadherent cells. The cells were then incubated overnight in α-MEM containing 10% fetal calf serum.

Myristoylation of Macrophage Proteins. Macrophages cultured at a density of approximately 3×10^6 cells per 35-mm culture dish were washed four times with PD and incubated for the indicated times in 1 ml of α-MEM containing [9,10-^{3}H(N)]myristic acid (20–40 Ci/mmol, New England Nuclear; 1 Ci = 37 GBq) and the specified stimuli. Stimuli included PMA (Sigma), *Escherichia coli* K-12 LPS (List Biologicals, Campbell, CA), monoacyl glucosamine phosphate (MAGP) (Lipidex, Middleton, WI), and zymosan (ICN) and were prepared, stored, and delivered as described previously (4). At the end of the specified incubation time the cells were washed three times with PD, and scraped into PD containing 1% (wt/vol) Nonidet P-40, 1 mM phenylmethylsulfonyl fluoride, aprotinin at 0.28 trypsin inhibitor unit/ml, 1 mM diisopropylfluorophosphate, and 15 mM EDTA (Sigma) (lysis buffer). Nuclei were removed by centrifugation for 5 min in an Eppendorf microcentrifuge and the protein content of the postnuclear supernatants was determined according to the method of Lowry *et al.* (16). Samples containing equiv-

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Abbreviations: 20:4, arachidonic acid; PMA, phorbol 12-myristate 13-acetate; LPS, bacterial lipopolysaccharide; MAGP, monoacyl glucosamine phosphate.

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15.May 85   GD3 (LIT) B17   (BRA)   F0408

LIPOPROTEINOSIS, ALVEOLAR

<u>Synonyms:</u>

pulmonary alveolar proteinosis, phospholipidosis, endogenous lipid pneumonia, pulmonary lipidosis, multifocal histocytosis, desquamative pneumonia (Weller et al., L119/F7)

<u>Lung Lesions:</u>

surface with white-gray spots, areas of alveoli filled with dense granular material and foamy macrophages. Material contains protein and lipid (cholesterol, triglyycerides and especially phospholipids). Additional cholesterol granulomas with giant cells, no indicators for inflammation

<u>Occurence:</u>

in humans, rats, hamsters and guinea pigs (Weller et al., L119/F7)

<u>Cause:</u>

related to inhaltion of dusts and aerosols (Weller et al., L119/F7)

chronic administration of chlorphentermine (Reasor et al., 1979, L9/J5)

intratracheal instillation of fly ash (Srivastava, P.K., Misra, U.K., Arch. Environ. Contam. Toxicol. 14 : 95-194 (1985a))

GD12 (LIT) A4

LIVER
=====

Renewal Time:

rat liver hepatocyte: 4oo to 45o days (MacDonald, Arch. intern. Med. 1o7: 335, 1961)

Cell Cycle Time:

rat liver hepatocyte: 48 h in 8-week old rat (Post and Hoffmann, Exp. cell Res. 63:111, 1964)

LIVER

Carcinogenesis:

According to a suggestion by Grasso (1979), the induction of the drug-metabolizing system (DMS) in the liver (or other organs) may represent a "work hypertrophy" as an adaptive response rather than a result of toxicity. In this case, the liver may be enlarged and histologically normal and the smooth endoplasmatic reticulum dilatated. Not-induced DMS accompanied by liver enlargement, depression of glucose-6-phosphatase, rER hypertrophy and - most important - lysosomal autophagy, however, are thought to indicate liver damage, which can lead to the development of carcinoma via nodular hyperplasia or adenoma. The nodular response represents possibly a reactive hyperplasia to sustained damage. The progression to carcinoma does not take place invariably, but occurs in a sufficient proportion to substantiate this hypothesis. The first case is observed after treatment with phenobarbitone, which was found to reduce the tumor incidence when administered simultaneously with liver carcinogens such as acetylaminofluorene. The order of administration seems to be important, since the protective effect was absent, when phenobarbitone was administered after the carcinogen. In this case the tumors were enhanced due to preferential stimulation of the growth of malignant cells (Grasso, 1979). Coumarin and xylidine (Pouceau MX) are representatives of the class of toxic compounds (Grasso, 1979).

Grasso, P., Liver growth and tumorigenesis in rats, Arch. Toxycol., Suppl.2: 171-18o(1979)

GD4 (LIT) B14 (LA)   29.May 81

LUCIFERASE

Luciferin + ATP + 1/2 O_2 Dehydroluciferin + AMP + PP + h

ATP-Bestimmungsmethode

Struktur von Luciferin:

Dehydroluciferin

GD13 (LIT) A2

LUMINOL
=======

3-aminophthalic acid hydrazide oxidized to 3-aminophthalic acid and emission of light

2028916583

2028916584

GD4 (LIT) B12 (LA)   29.May 81

MARKOVNIKOV REGEL

Bei der elektrophilen Addition von Protonsäuren an unsymmetrisch substituierte Olefine tritt das Wasserstoffatom an das wasserstoffreichste C-Atom der Doppelbindung.
Dabei entsteht als Zwischenstufe das stabilste Carbeniumion.

Beispiel: Addition von HCl an Propen

$$CH_3-CH=CH_2 + HCl \rightarrow \begin{cases} A: & CH_3-\overset{(+)}{C}H-CH_3 + \overset{(-)}{Cl} \\ B: & CH_3-CH_2-\overset{(+)}{C}H_2 + \overset{(-)}{Cl} \end{cases}$$

Das Kation A ist wegen des + I-Effekts der beiden benachbarten Methylgruppen stabiler als B. Als Endprodukt entsteht also Isopropy-chlorid.

MAST CELLS

Cytoplasmic Granules:

content: acid mucopolysaccharides,
histamine,
heparin,
5-OH-tryptamine,
chymotrypsin,
phospholipase A

Tumors:

mastcytoma: spontaneous cutaneous m. observed in dog (7 to 15 o/o of canine spontaneous skin tumors) (Cook, Natl. Cancer Inst. Monogr. 32: 267-283, 1969), (dg)

rarely seen in mice, (mu)

in man related to urticaria pigmentosa, (hu)

chemical induction by skin painting with: coal tar
2-methylcholanthrene
DMBA
cigarette tar

(Ohmori, T., Mori, H. and Rivenson, A., A study of tobacco carcinogenesis 2o, Mastocytoma induction in mice by cigarette smoke particulates ("cigarette tar"), Am. J. Pathol. 1o2: 381-387 (1981))

mastocytomas are benign tumors

Occurence:

resident in dermis.
Connective tissue: 2 types of mast cells differing in morphology, histochemical staining properties and location: (rt)
(1) normal conn. tissue mast cell
(2) mucosal mast cell: can be stimulated by parasites (e. g. helminth). Origin and relationship to (1) uncertain. Lymphocytes of infected rats may release factors causing pronounced mucosal mastocytosis (Haig, D.M., McKee, T.A. and Jarrett, E.E., Generation of mucosal mast cells is stimulated in vitro by factors dervied from T cells of helminth-infected rats, Nature 3oo: 188-19o, 1982)+.

GD1 (LIT) A5 LA (RZ) 4.Sep.81

MASTCYTOMA
==========

cf. MAST CELLS

GD11 (LIT) A24 WS 26.Nov.81

MDH
===

Plasma Half Life:

mMDH: 3o to 4o h (Smith et al., Release of mitochondrial enzymes (hu) in acute myo cardial infarction, J. Molecular Med. 2: 265-269, (1977)+)

GD4 (LIT) B9 (LA) 27.May 81

MELATONIN
=========

Epiphysenhormon

Chemie und Struktur:

Indolderivat, (Beziehung zum Serotonin)

Wirkung:

Aufhellung der Amphibienhaut
Antagonist des Melanotropins
Hemmung der Sekretion von Gonadotropen und ACTH
Tag-Nacht-Rhythmus (?) D1/3o7

GD4 (LIT) B8 (LA) 27.May 81

MELANOTROPIN, BETA MSH
======================

Hormon der Hypophyse:

Chemie und Struktur:

Produktion in der pars intermedia (Mittellappen)
Sequenz bekannt, ähnlich dem Corticotropin
Isolation und Sequenzanalyse: 1957 C.H. Li
18 AS, MG 2177, JEP 5,8

Rind: β_b-MSH Ser

Schwein: ß-MSH Glu (F/F, 1313)

Bereich 6-1o biologisch aktiv - wie bei ACTH und PH (Geiger S. 159)

Wirkung:

Amph. und Fische: Ausbreitung der Melanophoren in der Haut

Säuger:

ev. Förderung der Dunkeladaption,
Resynthese von Rhodopsin (D1/313, 33)

Proc. Natl. Acad. Sci. USA
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Cell Biology

Disulfide bonds and the translocation of proteins across membranes

(secretion/mitochondrial protein import/cysteine residues)

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Contributed by S. J. Singer, July 11, 1986

ABSTRACT **We are concerned with the mechanisms whereby hydrophilic proteins synthesized in the cytoplasm are translocated across one or two membranes into different cellular organelles. On the basis of a model of the translocation process to be described elsewhere, we propose an explanation of previous findings that the *in vitro* translocation across the endoplasmic reticulum of secretory proteins of higher eukaryotic cells appears to be obligatorily co-translational (i.e., occurs only while the polypeptide chain is being synthesized on the ribosome). We suggest that *in vitro* the intrachain disulfide bonds of the polypeptide rapidly form after it is released from the ribosome; the three-dimensional conformation of the chain is thereby stabilized and cannot undergo the unfolding that is required for post-translational translocation. In accord with this proposal, we show that the secretory preprotein human preprolactin, after translation and release from the ribosome, can indeed undergo translocation across endoplasmic reticulum membranes *in vitro* if the medium is sufficiently reducing. Those polypeptides that, in the absence of reducing agents, can be post-translationally translocated *in vitro* across bacterial, mitochondrial, and other types of membranes may generally lack intrachain disulfide bonds.**

Many of the membrane-bounded organelles in eukaryotic cells obtain most or all of their internal proteins from the cytoplasm. This generally involves the translocation of a wide range of large hydrophilic protein molecules from the cytoplasm across one or two membranes of the organelle. The mechanisms of such translocations have received a great deal of attention in the last decade, but they are still not well understood. In particular, while it would seem plausible that these mechanisms might be fundamentally the same in all such cases, the evidence until recently appeared to indicate that they were significantly different. Translocation of proteins across the endoplasmic reticulum (ER) of eukaryotic cells seemed to occur only while the polypeptide chain was being synthesized on ribosomes attached to the ER (i.e., translocation was obligatorily co-translational), whereas in other cases (bacterial, mitochondrial, peroxisomal, and chloroplast membranes) the polypeptide chain, after being completed and released from the ribosome, could generally be transported into the organelle (i.e., translocation could be post-translational). Of special significance have been *in vitro* studies demonstrating these differences, for example, between protein import into the ER of higher eukaryotic cells (co-translational) as compared to import into mitochondria (post-translational) (for reviews, see refs. 1 and 2).

We have developed a general picture of how protein translocation might work (3). This picture utilizes current ideas (4–7) about how the polypeptide chains of soluble proteins fold into their equilibrium tertiary structures. Briefly, our proposal involves the sequential translocation across the membrane of successive folded "subdomains" of the polypeptide chain until finally the entire chain is translocated. This process is initiated by the binding of the signal peptide, which is generally present at the amino terminus of the polypeptide chain, to a receptor in the appropriate membrane, which "seeds" (7) the formation of the first folded subdomain of the chain. As this subdomain is translocated across the membrane, the next stretch of the chain is folded into a second subdomain and is translocated. This energy-dependent process continues until the entire chain is transported across the membrane. For convenience, we refer to this mechanism as "subdomain translocation." In principle, this mechanism can function either co-translationally or post-translationally. In the latter case, the completed polypeptide chain that is released into the cytoplasm, still bearing its signal peptide, is presumably first rapidly folded into some tertiary conformation in the aqueous solution. If this polypeptide is subsequently to be transferred across a membrane by subdomain translocation, the tertiary conformation must be capable of being unfolded so that the initial and successive subdomains can be sequentially formed at the membrane and translocated. It occurred to us that if the released polypeptide chain, upon acquiring its tertiary conformation, also became rapidly cross-linked by intrachain cystine disulfide bridges, it would subsequently be incapable of unfolding to its subdomains; its post-translational translocation might thereby be blocked.

Let us pursue this suggestion further. The polypeptides that are translocated across the membrane of the ER in higher eukaryotic cells are mainly the precursors of secretory proteins, and it is known that most of these proteins contain multiple intrachain disulfide bridges. The cytoplasm of eukaryotic cells is highly reducing, because of its high concentration of glutathione (8); it is altogether likely that, after synthesis *in vivo*, secretory proteins do not become disulfide-bridged until after they are translocated across the ER membrane. In *in vitro* translocation experiments, however, such reducing conditions are normally not duplicated. If, in the *absence* of ER membranes, a secretory protein precursor was translated *in vitro* and released under oxidizing conditions, the intrachain disulfide bridges might form and, on subsequent addition of ER membranes, translocation would be blocked. On the other hand, if ER membranes and the required soluble factors were present during *in vitro* translocation, the nascent polypeptide chain, while being translocated across the membrane at its amino terminus, would still be attached to the ribosome towards its carboxyl terminus. Therefore, the complete tertiary conformation characteristic of the released molecule could not form as long as the nascent polypeptide was simultaneously attached and partly engulfed at its two ends; as a consequence, even under oxidizing conditions, the cysteine residues would probably be sufficiently separated from one another to remain reduced while synthesis and translocation of successive subdomains proceeded. The disulfide bonds would form only after most

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Abbreviations: ER, endoplasmic reticulum; m^7GMP, 7-methylguanosine 5'-phosphate.

27.Apr.82 GD6 (LIT) A3o WS

METASTASES

Definition:

Metastase muss vaskularisiert sein

Makro- und Mikrometastasen

Möglichkeiten der diskontinuierlichen Tumor Ausbreitung:

- lymphogen
- hämatogen (Leber, Lunge, Niere, Nebenniere, Gehirn, Lymphknoten)
- seröse Höhlen (Pleura, Peritoneum)
- iatrogene Verschleppung ("Impfmetastasen") durch Stichkanal und Schnittflächen von Operations-Geräten. Tumoren bleiben lokal!

nur ca. o.1 o/o der freigesetzten Zellen überleben und führen zu Metastasen. Die Bedeutung von Fibrin für die Anheftung der freigesetzten Zellen ist fragwürdig oder selten (Wiss. Kollog, Dr. Günther, Apr. 82)

GD55 (S) A3

METHYL METHANESULFONATE

Chemistry:

methylating agent

DNA Adducts:

7-MeGua, 3-MeAde and measurable amounts of O^6-MeGua in newborn rats, 2 h after i.v. adm. (Kleihues, P. et al., Z. Krebsforsch. 81: 273-283, 1974)+

RNA Adducts:

1-MeAde, 3-MeCyt and traces of O^6-MeGua (Kleihues, P. et al., Z. Krebsforsch. 81: 273-283, 1974)+

no metabolic activation, SN_2 agent (Kleihues, P. et al., Z. Krebsforsch. 81: 273-283, 1974)+

Carcinogenicity:

adult animals: very weak (Clapp et al., Science 161: 913, 1968), (Druckrey et al., Z. Krebsforsch. 74: 241, 197o)

neonate animals: malignant neurogenic tumors (Kleinhues et al., Europ. J. Cancer 8: 641, 1972)+

not hepatocarcinogen in rats (O'Connor, P.J. et al., Br. J. Cancer 27: 153, 1973)+

Half Life:

rat, in vivo: approx. 2o min (Swann, Biochem. J. 11o: 49, 1968)

Conjugation:

rapid conjugation to GSH (Kleihues, P. et al., Z. Krebsforsch. 81: 273-283, 1974)+

GD55 (S) A18   LA   (PW)   24.Aug.81

METHYLCHOLANTHRENE
=================

Radioact.-Labelled Mc:

G-3H 2o-Methylcholanthrene
185-55o GBq/mmol = 5-15 Ci/mmol   (Amersham TRK. 7o))

Structure:

CH_3

20-Methylcholanthren

24.Jun.85 GD8 (LIT) B24 (BRA)

METHYL-NITRO-NITROSOGUANIDINE (MNNG)
===================================

Stability:

labile compound (.LT.1 d, 37 degrees centigrade), more stabile at acid pH and frozen.

Adaptation:

low conc. (0.5 or 1 ug/ml) of MNNG can lead to adaptation of E. coli to challenge by higher conc. of MNNG (e. g. 10 to 50 ug/ml) or by other mutagens = formation of less mutations. Adaptation may be related to the prevention or excision of O-6-methylguanosine from DNA by "adaptation enzyme(s)". No change of growth rate. Simultaneously resistance to MNNG-killing. (Vortrag Jeggo, Dez. 1979, Essen)

Carcinogenicity:

oral administration cause cancer of the glandular stomach in rats (CaD, p. 100)

GD55 (S) A2 (PW)

METHYLNITROSOUREA
================

Ultimate Carcinogenic Metabolite:

methyl cation produced by metabolism or chemical breakdown in vivo, SN_1 agent (Kleihues, P. et al., Z. Krebsforsch. 81: 273-283, 1974)

Target organ:

brain
(Swann, Magee, Biochem. J., 110: 39, 1968)

MICROSOMES

==========

Isolation by gel filtration:

(1) Sepharose CL-2B
2.5 cm x 3o cm column
buffer: o.25 mol/l sucrose/5o mmol/ Tris-HCl/25 mmol/l KCl/5 mmol/l MgCl2/1 mmol/l EDTA, pH 7.5
temperature: 1 to 4 degrees centigrade
flow rate : 2o to 3o ml/h
sample : 2.5 ml postmitochondiral SN

(2) Bio-Gel A15om
1 cm x 22 cm column
buffer : as (1)
temperature: 1 to 4 degrees centigrade
flow rate : 5 ml/h
sample : 1 ml postmitochondrial SN

GD82 (S) B23 LA (PW) 26.Aug.81

MICROSOMES
==========

<u>Purification:</u>

Gel filtration: (McCole, N., Palmer, D. N. and Williams, D. J., Biochem. J. 18o: (2) 437-439, 1979,
Mishin, U.M., Grishanova, A. Y. and Lyakhovich, V. V., Febs. Lett. 1o4: (2) 3oo-3o2, 198o,
Miks, B., Kawiak, J. and Hoser, G., Folia.Histochem. Cytochem. (Krakow), 16: (3) 187-92, 1978)

GD6o (S) A 22

MISHELL-DUTTON SYSTEM
=====================

complete in vitro antibody production after antigen stimulation, Ab production dependant upon presence of serum (FCS), mercapto-aethanol or MASF (serum factor). Mouse serum not applicable, since cytotoxic to spleen cells (Vortrag.Opitz, 25.Oct.1979)

GD58 (S) A12

MITOMYCIN C
===========

Mutagenic Action:

cross-linking of DNA (Green, M.H.L., Arch. Toxicol. 39 : 241-248, 1978)

GD78 (S) B13 (LA)   29.May 81

MITOSE-REGULATION
=================

1. Kern-Plasma Relation (gilt.nicht allg.)

2. Wundhormone

3. Traumatinsre. (Bohnenhülsen)

4. Cycl. AS; bes. Tyrosin

5. Cytokinesin I:

Cytokinin + Cytokinesin I (–) Phosphodiesterase cAMP
(Ref: cAMP)   ständige Zellteilung
(gewebekult. von Vinca
rosea)

fanden beim $[P(CN)_2Br_2]^-$ die ψ-trigonal-bipyramidale Struktur, die man aufgrund der VSEPR-Theorie erwartet. Beim $[P(CN)_3Br]^-$ stellten sie ψ-oktaedrische Koordination in einer dimeren Struktur mit Bromid-Doppelbrücken fest und beim $[PBr_4]^-$ eine intermediäre Struktur zwischen diesen beiden. Bei ihm ist die trigonal-bipyramidale Koordination in Richtung auf eine tetraedrische Geometrie verzerrt. Das steht im Widerspruch zur VSEPR-Theorie und kommt wahrscheinlich durch Ligand-Ligand-Abstoßung zustande. Die Strukturen sind als Modelle für den Übergangszustand bei nucleophilen Substitutionen am Phosphor(III) interessant. [J. Chem. Soc. Dalton Trans., im Druck]

Die Umwandlung eines Allens in ein μ-Dimethylcarben an einem Dirutheniumzentrum gelang A. F. Dyke et al. Der Dimetallocyclus *(1)*, in dem sich die $C_2(C_6H_5)_2$-Einheit leicht gegen Acetylen oder 2-Butin austauschen läßt, reagiert mit Allen – ebenfalls unter Freisetzung von Diphenylacetylen – quantitativ zu *(2)*. Daraus erhält man nach dem Ansäuern mit HBF_4 und Behandlung mit Natriumtetrahydridoboran bei −78 °C

(1) $\xrightarrow[-C_6H_5-C\equiv C-C_6H_5]{CH_2=C=CH_2}$

(2) $\xrightarrow{HBF_4}$

(3) BF_4 $\xrightarrow{NaBH_4}$

(4)

den μ-Dimethylcarben-Komplexe *(3)* in 60-proz. Gesamtausbeute. Die Reaktionssequenz ist ein neuer, bequemer Zugang zu Carben-Komplexen. [J. Organomet. Chem. *199*, 647 (1980)]

Zellmotilität

Die gezielte Fortbewegung lebender Zellen ist auf verschiedene Weise möglich. Am allgemeinsten bekannt ist die Bewegung mit Hilfe von Flagellen und Cilien, die man z. B. bei der Schwimmbewegung der Bakterien oder bei den wellenartig sich bewegenden Cilien im menschlichen Bronchialgang vorfindet. Amöben, Makrophagen und andere weiße Blutkörperchen bewegen sich durch geordnete Formveränderungen fort. Dabei wird z. B. zusammen mit einer gerichteten Verschiebung des Zellinhalts auch die Zellaußenmembran verschoben, so daß sich die Zelle gerichtet fortbewegt. Bestimmte kultivierte Zellen tierischen und menschlichen Ursprungs, die an Glas- und andere Oberflächen anhaften, können sich durch alternatives Anhaften und Ablösen fortbewegen. Eine wichtige Rolle bei diesem Prozeß spielt die gefurchte (ruffled) Membran, die sich an der Haftstelle befindet und entsprechend an- und abgebaut wird. Man vermutet, daß sich tierische Zellen auf ähnliche Weise im Zellverband, also auch im Körper fortbewegen können. Hauptsächlich verantwortlich für diese Form von Bewegung und Formveränderung sind die Mikrofilamente, die im wesentlichen aus Aktin und Myosin bestehen. Bis zu 30 % des Gesamtproteingehaltes von Amöben oder bewegungsaktiven weißen Blutkörperchen sind daher Aktin. Die bei einigen Zellen beobachtete sprunghafte Weise der Bewegung wird derzeit nur wenig verstanden.

In den meisten Fällen kommt die Bewegung von Muskel- wie von Nichtmuskelzellen durch die Wechselwirkung von Aktin und Myosin zustande, wobei außerdem noch ATP als Energiequelle benötigt wird. Gewöhnlich wird Bewegung durch ein System von Mikrofilamenten bewirkt, welches über- und untereinander gleitet. Die Bewegung nichtbakterieller Cilien und Flagellen funktioniert auf ähnliche Weise, wobei jedoch die Proteine Tubulin und Dynein die Stelle von Aktin und Myosin einnehmen. Muskelzellen und andere zur Bewegung fähige Tierzellen unterscheiden sich dadurch, daß Aktin und Myosin in ersteren in Sarcomere genannte feste Strukturen eingebaut sind, während die Filamentstrukturen von Nichtmuskelzellen je nach Bedarf Netzwerke ausbilden und abbauen. Ein besonders auffälliges Beispiel hierfür ist die durch Aktin-Myosin-Filamentnetzwerke besorgte Ausrichtung der Chromosomen vor der Zellteilung und das folgende Auseinanderziehen der Zelle von den Polen aus. Aus kürzlich von E. D. Korn und Mitarbeitern vom National Heart, Lung and Blood Institute veröffentlichten Berichten in „Nature" und „Proceedings of the National Academy of Sciences" geht hervor, daß es möglicherweise in ein und derselben Zelle verschiedene Formen von Myosin gibt, die für verschiedene Bewegungsabläufe zuständig sein könnten. Wichtige Erkenntnisse zum molekularen Mechanismus der Zellbewegung kommen aus der Arbeitsgruppe von T. P. Stossel vom Massachusetts General Hospital. Nachdem diese vor einigen Jahren das „actin binding protein" entdeckt hatte, das im Innern der Zelle die Aktinfilamente verankert, hat sie kürzlich in „Nature" das Protein Gelsolin beschrieben, das zellinterne Aktinstrukturen auflösen kann. Im Oktoberheft von „Cell" beschreiben nun M. Crumet und S. Lin von der Johns Hopkins University erstmals auch ein Protein, das für die Ausbildung und Auflösung von aktinhaltigen Filamenten in Nichtmuskelzellen mitverantwortlich zu sein scheint.

Es ist erst etwa 15 Jahre her, daß P. Satir erstmals gleitende Mikrotubuli als Grundlage der Cilienbewegung nachweisen konnte. Weitere wichtige Stationen zum heutigen Verständnis der Zellmotilität waren die Versuche von G. Albrecht-Bühler vom Cold Spring Harbor Laboratory, der die von Zellen in Zellkultur zurückgelegten Wegstrecken erstmals sichtbar machen konnte, und jene der Arbeitsgruppe um N. K. Wessels aus Stanford, die die entscheidende Rolle der Filamente und Tubuli bei den Formänderungen von Zellen nachwiesen. Die klarste Demonstration der zellinternen Netzwerke von Mikrofilamenten und Tubuli stammt aus dem Labor von K. Weber, Göttingen, der mit Hilfe von fluoreszenzmarkierten Antikörpern gegen Aktin diese Netzwerke sichtbar machen konnte.

Der rasche Fortschritt bei der Aufklärung der Mechanismen der Zellbewegung wurde auch durch ihre Bedeutung für die Funktionen des Lebens verursacht. So kommt z. B. erst durch definiert gerichtete Bewegung die Differenzierung der befruchteten Eizelle zum komplexen biologischen Organsystem zustande. Fehler in diesem Bewegungsablauf sind andererseits wohl die Ursache für Störungen in der Embryonalentwicklung. Viele menschliche und tierische Zellen zeigen, wenn sie in Kultur auf Petrischalen gehalten werden, das Phänomen der Kontaktinhibierung. Hierunter versteht man das Anhalten der Zellbewegung (und des Zellwachstums) bei Berührung einer benachbarten Zelle. Gerade in diesem Mechanismus unterscheiden sich viele Tumorzellen von normalen Zellen, indem sie nämlich trotz Zellkontakt aggressiv weiterwachsen und so in gewebefremde Bereiche eindringen. Viele mit der Immunabwehr beauftragten Zellen sind imstande, im Blut zirkulierende Fremdmaterialien zu binden und in sich aufzunehmen. Auch diese vitale Funktion kommt durch gerichtete Zellformveränderung zustande, und es ist daher klar, daß ein Verständnis dieser Mechanismen weitreichende Implikationen sowohl für unser Verständnis eines grundlegenden biologischen Phänomens wie auch für viele praktische medizinische Problemkreise hätte.

A. M.

24.Jan.83 GD97 (S) B21 PS

MUSCLE CONTRACTION (1)

Ruhe-Membranpotential: - 90 mV

Leitungsgeschwindigkeit: 5 m/s

abs. Refractärzeit: 1 bis 3 ms

Reizschwellen: Nachpolarisation u. Schwellenveränderungen dauern relativ lang

Schwellenunterschiede bestehen zwischen einzelnen Fasern und die Entfernung zwischen Reizelektrode u. Faser wirkt sich ebenfalls aus.

Ionenkonzentration (Gleichgewicht):

Ion	Konz. (mMol/l) intrazell	extrazell
Na	12	145
K	155	4

Depolarisation: Na^+-Influx
Beginn an der motorischen Endplatte

Repolarisation: K^+-Efflux

Auslösung der Kontraktion/ (Erregungs-Kontraktionskopplung): durch das über die Muskelfaser fortgeleitete Aktionspotential

Einzelzuckung: Beginn: ca. 2 ms nach Beginn der Polarisation, vor vollendeter Repolarisation

Dauer: 8 bis 100 ms

Auftreten in vivo:
nur bei Dehnungsreflexen

Isometrische Kontraktion: ohne sichtbare Verkürzung des Muskels

Isotonische Kontraktion: ohne Veränderung der Spannung bei gleicher Gegenlast, mit Verkürzung

24.Jan.83 GD97 (S) B22 PS

MUSCLE CONTRACTION (2)
=================

Auxotone Kontraktion: Mischform von isometr. u. isotonischer K., annähernd in vivo Situation.

Muskelarbeit: Kraft x Weg

Tetanus: Summation von Kontraktionen
- unvollständiger T.
- kompletter T.

notwendige Frequenz (= Fusionsfrequenz, Warmblüter: 5o-1oo Hz)

Ermüdung (Anhäufung von Metaboliten) führt zur Abnahme der Fusionsfrequenz

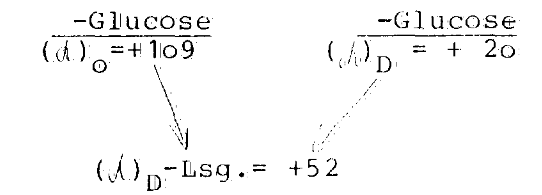
Art der Kontr.-Messung bei A-/1629: auxoton, da zwar konst. Gegengewicht (8 g), jedoch am Biegestab Feder, die nur 2-5 mm Auslenkung zulässt. Bei Fixierung dieser Feder (Auslenk. ≈ O) würde die Kontr.-Amplitude die Schreibpapierbreite (8 cm) überschreiten.

GD78 (S) B7 (LA) 29.May 81

MUTAROTATION

= allmähliche Veränderung der optischen Drehung, wenn reine α- und β-Glucose in H_2O gelöst werden.

(Gleichgewichtseinstellung!)
37 o/o α, 63 o/o β



Schnelle Gleichgewichtseinstellung, wenn Säure und Base vorhanden sind; z.B. Phenol und Pyridin (C4A/510)

GD57 (S) A1o (LA) 21.Apr.81

MYCOPLASMA (1)
==========

Inhibitors:

Tyonine (?)
Lincomycine (better than Tyonine)
but resistance to Ampicillin and Penicillin

Identification:

(1) growth on selective media: facultative anaerobic, sterol requirement (horse serum)
(Flow Laboratories, catalog)

(2) Assay with BuDR (?):
Prof. Rajewski, Köln

(3) visualization by autoradiography:
Very high 3H-thymidine incorporation

(4) staining with fluorescence dye (Hoechst)

(5) immunofluorescence

Localization on/in infected cells:

most probably adhesion to outer cell surface

Removal from cultured cells:

not possible by sterile filtration because of small size (o.3 micrometers)

method developed by Dr. Peters, Köln: mouse peritoneal macrophages, grown to confluent layer remove mycopl. from cells within a few days. To be published in Nature.

Commercially available strains:

M. arginini
M. pneumoniae, Flow Laboratories

Effect of Hepes:

induction of bigger colonies

MYCOPLASMA (2)
==========

Mycoplasma Pneumoniae:

pathogenesis poorly understood, activation of C1, C2, C3 and C4 in bronchial secretions shortly after intranasal infection (guinea pig). Activation may represent unspecific defense before the specific immune response; complement is activated via the classical and alternative pathway in the absence of antibodies. 2 weeks after infection serum antibody titer increased up to 6 weeks (Loos, M., Brunnen, H., Infection and Immunity 25: 583-585, 1979)Li

guinea pigs)
hamsters) highly sensitive to M. pn.

Lung Lavage:

recovery of living organisms (Brunner, Colloq. Inst. Natl. Santé Rech. Med. 33: 411-42o, 1974)

recovery not possible with buffered saline but with sterile broth medium (Loos, M., Brunnen, H., Infection and Immunity 25: 583-585, 1979)

GD78 (S) B6 (LA) 27.May 81

MYOKINASE
=========

<u>Catalyzed Reaction:</u>

$2\ ADP \rightarrow ATP + AMP$

GD6o (S) A28

MYOPATHY
========

muscle pathology of non-neurogenic origin i.e. genetic or in-flammatory diseases.

differentiation by lack of serum enzyme changes in neurogenic muscle diseases.

NO

2028916609

8.Aug.83 GD14 (LIT) B16

NERVE GAS
=========

gas for chemical warfare

"irreversible" cholinesterase inhibitors

example: diisopropyl fluorophosphate

25.Jul.84 GD15 (LIT) B25 (RZ)

NEUTROPHILIA
============

Causes:

- without left distortion: stress-related
- with left distortion: due to bacteria, endotoxins
(Piper, p. 403)

GD27 (S) B25 (PW)

N-NITROSODIMETHYLAMINE
=====================

Alkaline elution:

nitrosodimethylamine increases rate of elution from liver, kidney and lung, but not from brain nuclei. (Parodi et al., Mutat. Res. 54: 39-46, 1978+) (mu)

2028916612

GD69 (S) A1 (PW)

NORADRENALINE
=============

Assay:

The availability of S-adenosyl-L-(methyl-3H)methionine(3H-SAM) at very high specific activity has made possible the development of a highly sensitive and specific radioenzymatic assay for catecholamines. The basis of assay is either to O-methylate or to N-methylate the catecholamines in biological systems using catecholamine-O-methyl transferase (COMZ) or phenylethanolamine-N-methyl transferase (PNMT) respectively with 3H-SAM as the methyl donor. After methylation the individual catecholamines, as their methyl derivatives, are separated and quantified. Amersham research news 9, 1981)

2.Dec.86 GD11LITA15

NORHARMAN
=========

Mechanism:

not capable of intercalating with DNA. Mode of action probably dependent upon ability to inhibit certain MFO enzymes in the S9 fraction employed with in vitro mutagenicity assays
(Wakabayashi et al., Mutat Res. 80 : 1-7 (1981)+)

Inhibition of conversion of hydrophobic to hydrophilic B(a)P metabolites. Large amounts of phenol, quinones and diols as well as the strong mutagen 7,8-dihydroxy-B(a)P (10-fold increase) formed. The latter may be the major reason for the commutagenic action of norharman in the Ames assay
(Nagao et al., Biochem. Biophys. Res. Commun. 83 : 373-378 (1979)+)

Comutagen with o-toluidine
(Sugimura, Int. Congr. Toxicol., Tokyo, 1986)

DRWK
-- Daten, Information

PRODUCT ANALYSIS REPORT

Product: Oligo (dT)-Cellulose Type 2

Catalog No: 20002

Lot No: 770-52

Cellulose: Whatman CF-11, washed with a modification of the procedure of Alberts and Herrick, Methods in Enzymology, Vol XXI, 198, (1971).

Oligo (dT): Chains of up to 18 nucleotides long, covalently attached via the terminal 5'-phosphate.

Poly (rA) binding: 46.5 OD_{260} per gram

Binding buffer: 0.5 M NaCl, 0.01 M Tris (pH 7.5).

Elution buffer: 0.01 M Tris (pH 7.5).

RNA binding: 93 % [^{3}H]-mRNA from HeLa cells

Binding buffer: 0.5 M NaCl, 0.01 M Tris (pH 7.5) 0.5% SDS, 1mM EDTA

Elution buffer: 0.01 M Tris (pH 7.5), 0.05% SDS, 1mM EDTA

Analyzed by: [signature]

Stability: 3-6 Months

Date: 4/11/78

2028916615


Research Products Division
Collaborative Research, Inc.
1365 Main Street, Waltham, Mass. 02154

Tel: (617) 899-1133 Cable: Collabres TWX: 710-324-7609

DRWK

Oligo(dT)-cellulose
Storage Conditions

1. Oligo(dT)-celluloses are shipped at ambient temperatures. Upon arrival the celluloses should be stored at -20°C. Refrigeration at 4°C is adequate only for short periods of time.

2. Prolonged storage (up to six months) is best at -70°C. Oligo(dT)-celluloses are not guaranteed stable, even at -70°C, for more than six months.

3. After use, the oligo(dT)-cellulose should be washed extensively with eluting buffer to remove all traces of bound material. If the column is to be stored at 4°C for several days, 0.2% sodium azide or chloroform saturated buffer should be passed through the column to stop possible bacterial contamination.

4. Prolonged storage of used cellulose should be at -20°C as a dry solid. After use, the column should be washed first with 0.1N sodium hydroxide, then water, and finally absolute ethanol. It is pumped dry under vacuum overnight. The dry powder can then be sealed in a plastic container and stored at -20°C or -70°C.



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25.Sep.84 GD15 (LIT) B29 (RZ)

OPZONIZATION
============

Definition:

modification of cells by binding of antibodies, complement components (e. g. C3b) etc., which facilitate the phagocytosis of these cells.

IgM and IgA do not opsonize by themselves, but via activation of C3

IgG, C3b: specific opsonization
fibronectin: unspecific opsonization

GD55 (S) A21

OSMOLALITÄT
===========

osmolare Konz. pro kg H_2O (angegeben in Osmol/kg H_2O) e: osmolality

(Reallexikon der Medizin, 5. Band, München-Berlin-Wien: Urban & Schwarzenberg, 1973)

GD55 (S) A22

OSMOLARITÄT
===========

Mass der osmotisch wirksamen Konz., bezogen auf die Vol.einheit einer Lösung; bei Nichtelektrolyten mit Molarität identisch; bei dissoziierten Stoffen = Molarität x Zahl der Ionen in 1 Mol; angegeben in Osmol/l Lsg. e: osmolarity
(Reallexikon der Medizin, 5. Band, München-Berlin-Wien: Urban & Schwarzenberg, 1973)

GD69 (S) A8 (PW)

OUABAIN
=======

Lymphocyte activation: (hu)
inhibition of activity, ConA-binding unaffected but incorporation (rb)
of unsaturated fatty acids into membrane phospholipids inhibited.
(Vortrag Resch, 16. Mar. 81)

GD56 (S) A2o

OXYGEN (1)

Blood Oxygen:

arterial: 15-23 Vol. o/o
venous: 1o-18 Vol. o/o

- content = in vivo conc. of O_2
- capacity = max. quantity
- saturation = ratio of content to capacity (o/o)
- tension = arterial 83-1oo mm

Physical Solubility:

3 microl./ml blood x mm oxygen pressure
(Handbook of clin. lab. data, p. 315-17)

at 76o Torr:

2o degrees centigrade: 3.11 ml/1oo ml
1oo degrees centigrade: 1.7 ml/1oo ml

Determination in Blood:

sampling of arterial blood from ear: treatment with Finalgon forte (v. Ardenne, M., GIT, Labor-Medizin 4 : 269-38o, 1979)

pO2 in Blood:

dependent upon daytime, age, caffeine, smoking, stress, training, influenza.

indication for circulation reserves (v. Ardenne, M., GIT, Labor-Medizin 4 : 269-38o, 1979)

reduction of risk during aging: 3 step treatment: (1) increase of O_2 utilization by vitamin B_1-therapy, (2) exposure to 4o o/o O_2, (3) training and (4) reduction of HbO_2 binding by phytinic acid treatment ((v. Ardenne, M., GIT, Labor-Medizin 4 : 269-38o, 1979)

Determination in Muscle:

implantation of oxygen permeable Silastic tube connected to blood gas analyzer via Nylon tubing. Infusion of hypoxic saline (o.o7 ml/min) through tubing (Niinikoski, J., Halkola, L. in Silver, I.A., Erecińska, M., Bicher, H.I. (Eds.): Oxygen Transport to Tissue 3, New York: Plenum Press, 1978, pp. 585-592)

24.Jan.83 GD97 (S) B19 PS

F0434

OXYGEN
======

Artificial Oxygenation:

fluorocarbons used for cell-free perfusion media

2028916622

24.Nov.82 GD97 (S) B3 WS

OXYGES SATURATION
================

Determination of Binding Curves:

Dr. Sick (Biologe)
Abt. Physiol. Chemie
RWTH Aachen
(o241) 42189143

apparatus suitable for complete analysis within 1o min, rat hemoglobin tested already.

PQ

PARTICLES
=========

TLV:

for nuisance particulates containing .LT.1 0/0 quarz: 5 mg/m3 equiv. to 5 ug/l (American Conference of Governmental Industrial Hygienists (ACGIH), Threshold limit values for chemical substances and physical agents in the work environment with intended changes for 1982, ACGIH, Cincinnati, Ohio, 1982)

Permeability of the Endothelial and Epithelial Barrier to Albumin Flux in the Sheep Lung, Stewart, Paul A.**, and Gorin, A.B., U.C. Davis, Davis, Calif. 95616

We studied 15 sheep with chronic lung lymph fistulas and measured the time course of the normal flux of albumin between the plasma and broncho-alveolar lumen (BAL) under baseline conditions. Fractional equilibration of tracer in the BAL and pulmonary interstitium (IS) were determined at varying times after intra-arterial injection of 100 μCi I^{125} albumin at t=0. Equilibration occurred in the airfilled lung. Luminal fluid was sampled using the fiberoptic bronchoscope. We measured protein bound radioactivity and albumin content of all samples (plasma (P), lymph (L), and alveolar lavage fluid (A)). The $t_{1/2}$ for albumin in the alveolar lavage was 16.6 hours (r=-0.97) compared to a normal $t_{1/2}$ of 2.4-3 hours in pulmonary lymph.

Minutes after t_0	15-40	215-445	1310-1775	2490-3315
n=	12	13	13	14
[A]/[P]*	2.3±.3	6.5±1.4	20.9±3.4	57.3±3.0
[A]/[L]*	0	16.1±.03	23.3±.06	73.2±.06
[L]/[P]*	10.6±3.1	44.5±3.3	97.9±8.1	---

*[CPM/gm albumin], ratio X 10^{-2} ± S.E.M.

We conclude that the plasma proteins present in alveolar lavage fluid reach the alveolar space by a normal diffusive process, not as a result of epithelial damage occurring at the time of lavage. Although lymph and plasma are substantially equilibrated within 24 hours, the BAL has not reached equilibrium with either the vascular or IS compartment at 48 hours after tracer administration. In the airfilled lung, albumin flux into the BAL is characterized by 2 exponential phases. Movement of albumin across the epithelial barrier in phase 1 (lasting 24 hours) is slower than in phase 2. (Supported in part - USPHS Pulmonary SCOR grant HL 19155). ** ALA Clinical Fellow

-> 1564 -> 1kW4

AMERICAN THORACIC SOCIETY 1905

ANNUAL MEETING SUPPLEMENT

Program and Abstracts

Volume 117
Number 4
April 1978
(part 2 of 2 parts)

Respiratory Disease

AMERICAN LUNG ASSOCIATION
AMERICAN T... SOCIETY
CONGRESS OF L... ION STAFF
ANNU...
R...

Boston, Mas...

S. 155u, S.156, 59o, 61u, 165u, 167, 71u, 80o, 84u, 106o, 219o, 236u, 238u, 240, 245u, 250o, 254o, 259, 266o, 269o, 271o, 273o, 306u, 319u, 320u, 327u, 335o, 341u, 352u, 353o, 360u, 403o,

bitte angegebene Seiten für mich kräuskopieren.

-> FJA Loh, 12.6.78

60, 72 u 220 u 220.

2028916627

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→FJA Loh, 12.6.78

60o, 72u 220u 220o

2028916627

GD55 (S) A12

PEROXIDASE
==========

Assay:

peroxidase forms with hydrogen peroxide, MBTH and DMAB a deep purple compound.

sensitivity: picomolar range (Ngo, T.T., Lenhoff, H.M., Anal. Biochem. 1o5: 389-397, 198o) +

GD55 (S) A7

PEROXIDASE ACTIVITY
==================

Macrophages:

activity can be determined cytochemically in resident macrophages including lung.

rabbit and human lung:
lavaged macrophages show activity in cytoplasmic granules (probably involved in antimicrobial activity.

rat lung:
2 populations, 1 with activity in rough ER (function not known), nuclear envelope and cytopl. granules, 1 with activity only in granules (Shimosato et al., Recent Adv. RES Res. 12: 73, 1972)

guinea pig lung, mouse peritoneum:
2 populations: 1 with activity in r. ER and nuclear envelope (= "resident"), 1 with activity in granules (= "monocyte derived")

21.Sep.87 RWA/BRA GD3LITA9

PEROXISOMES
===========

Proliferation

Proliferation of peroxisomes was determined biochemically using the cyanide-insensitive palmitoyl CoA oxidation assay (PCO), which is specific for peroxisomes and is a quantitative indicator for peroxisome proliferation.
(Golsworthy and Popp, CIIT Activities 7 (8), 1987)